Timing and location of blood product transfusion and outcomes in massively transfused combat casualties

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BACKGROUND: Hemostatic resuscitation using blood components in a 1:1:1 ratio of platelets:fresh frozen plasma:red blood cells (RBCs) is based on analyses of massive transfusion (MT, ≥10 RBC units in 24 hours). These 24-hour analyses are weakened by survival bias and do not describe the timing and location of transfusions. Mortality outcomes associated with early (first 6 hours) resuscitation incorporating platelets, for combat casualties requiring MT, have not been reported.

METHODS: We analyzed records for 8,618 casualties treated at the United States military hospital in Baghdad, Iraq, between January 2004 and December 2006. Patients (n 414) requiring MT, not receiving fresh whole blood, and surviving at least 1 hour (reducing survival bias) were divided into 6-hour apheresis platelet (aPLT) transfusion ratio groups: LOW (aPLT:RBC, ≤0.1, n 344) and HIGH (aPLT:RBC, >0.1, n 70). Baseline characteristics of groups were compared. Factors influencing survival on univariate analysis were included in Cox proportional hazards models of 24-hour and 30-day survival.

RESULTS: Patients received aPLT in the emergency department (4%), operating room (45%), intensive care unit (51%). The HIGH group presented with higher ($p < 0.05$) admission International Normalized Ratio (1.6 vs. 1.4), base deficit (8 vs. 7), and temperature (36.7 vs. 36.4). Overall mortality was 27%. At 24 hours, the HIGH group showed lower mortality (10.0% vs. 22.1%, p 0.02). Absolute differences in 30-day mortality were not significant (HIGH, 18.6%; LOW, 28.8%, p 0.08). On adjusted analysis, the HIGH group was independently associated with increased survival: LOW group mortality hazard ratios were 4.1 at 24 hours and 2.3 at 30 days compared with HIGH group (p 0.03 for both). Increasing 6-hour FFP:RBC ratio was also independently associated with increased survival.

CONCLUSION: Early (first 6 hours) hemostatic resuscitation incorporating platelets and plasma is associated with improved 24-hour and 30-day survival in combat casualties requiring MT. (*J Trauma Acute Care Surg*. 2012;73: S89 S94. Copyright © 2012 by Lippincott Williams & Wilkins)

LEVEL OF EVIDENCE: Therapeutic study, level III.

KEY WORDS: Apheresis platelets; resuscitation; massive transfusion; combat trauma.

Since Damage Control surgery was codified by Rotondo and Schwab in 1993,[1] blood use in trauma care has changed considerably, in large part because of the United States military experience in Iraq and Afghanistan.[2] United States military reports of decreased mortality in massive transfusion patients (MT, ≥10 red blood cell [RBC] units in the first 24 hours) associated with transfusion of fresh frozen plasma (FFP) and RBCs in a 1:1 ratio prompted the rewriting of MT protocols to incorporate the earlier empiric use of plasma in the care of exsanguinating patients.[3] Similarly, United States military reports of decreased MT patient mortality associated with increased transfusion of apheresis platelets (aPLT) led the United States Army Surgeon General to mandate platelet availability in theater.[4] APLT were first introduced in theater in January 2004. APLT collection capability is now in place at every Army Combat Support Hospital and Blood Support Detachment. The United States military experience has been corroborated by civilian studies.[5–9] Modern MT protocols incorporate the empiric use of platelets, plasma, and RBCs, generally in a 1:1:1 ratio, a practice that has become the cornerstone of damage control resuscitation.[5,10] The evidentiary basis for these protocols is weakened by the fact that the clinical studies supporting their implementation are retrospective and suffer from survival bias.[11] The problem of survival bias was described by Snyder et al.[12] who showed that analyzing the FFP:RBC ratio in civilian MT patients as a time-varying covariate rather than as a fixed ratio at 24 hours erased a statistically significant survival benefit. These authors found that plasma and other components were administered late in resuscitation and did not play a significant role in early treatment and outcomes. Nevertheless, recent reports from civilian trauma centers have shown that higher aPLT:RBC and FFP:RBC ratios in the first 6 hours of resuscitation, the period during which most trauma death occurs, retain the association with decreased mortality seen in analyses of resuscitation for 24 hours.[8,13–15] This suggests that the retrospectively observed benefits of hemostatic resuscitation may be real and not simply caused by survival bias. Larger recent studies using time covariate adjustment for

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survival bias still report improved outcomes with higher ratios of plasma and platelets to RBCs in patients with severe traumatic injury.[6,16] Here, we describe transfusion in the first 6 hours of resuscitation of combat casualties, a unique population of severely injured trauma patients, to present an analysis that minimizes survival bias and provides sufficient detail of transfusion timing and location to facilitate improvement in resuscitation protocols. Our analysis focuses on the impact of platelet transfusion, as platelets have the shortest shelf life of any blood component and are the most difficult to provide on the battlefield.

PATIENTS AND METHODS

Patients

We conducted a retrospective review of casualties admitted directly to the United States combat support hospital in Baghdad, Iraq (Ibn Sina Hospital), between January 2004 and December 2006 and analyzed transfusion patterns and mortality outcomes in patients who received an MT (≥10 units of RBCs within 24 hours). Patients included United States military personnel, Coalition Forces personnel, and Foreign Nationals. The primary end points were survival at 24 hours and at 30 days. We excluded patients who were transferred from other facilities, who received their MT for reasons other than initial resuscitation of trauma-induced hemorrhage (e.g., after the excision and grafting of burns) and patients whose records were not evaluable. Because it is not known whether platelets contained in fresh whole blood (FWB) are equivalent to aPLT, we excluded patients receiving FWB. Finally, we excluded patients who died within 1 hour of presentation to further reduce survival bias.

Patients (n = 414) who met the inclusion criteria were divided into two groups defined by 6-hour platelet transfusion ratios: LOW, 1:10 or less aPLT per stored RBC unit, aPLT:RBC, and HIGH, more than 1:10 aPLT:RBC. A 1:10 threshold of aPLT to RBC units was chosen based on previous analysis by Perkins.[4] Because one aPLT unit has been equated to five units (range, 4–6 units) of whole blood–derived platelets, a ratio of 1:10 of aPLTs to RBC units is similar to 5:10 or 1:2 of whole blood–derived platelets to RBC units. Therefore, the HIGH group is similar to 1:2 or higher of whole blood–derived platelets to RBCs. The use of a 1:2 ratio as a threshold to define high and low ratios of blood products has been used previously for both plasma and platelet related analyses.[14]

Data Sources

This study was conducted under a human use protocol that received institutional review board approval at the Brooke Army Medical Center, Fort Sam Houston, Texas. MT patients and the blood products they received were identified by querying transfusion records maintained within the Department of Defense Armed Services Blood Program Office (ASBPO) database in Falls Church, Virginia. Baseline patient demographics and outcomes were obtained from the Joint Theatre Trauma Registry (JTTR) maintained at the United States Army Institute for Surgical Research, Fort Sam Houston, Texas. Data from outpatient visits of United States military casualties discharged from the hospital before 30 days were abstracted from the Joint Patient Tracking Application. Mortality and dates of death were verified by cross-referencing military records with the Social Security Death Index and the listing of casualties provided on the Iraq Coalition Casualty Count Web site (www.icasualties.org).

Patient charts were reviewed by 2 physicians (A.P.C. and J.G.P.) to cross-reference and verify vitals, laboratory reports, blood product transfusions, and outcomes. Charts were analyzed directly or by using the Patient Administration Systems and Biostatistics Activity system, which compiles all inpatient records from deployed medical units. Blood component administration timing and location were extracted from the chart and were cross-referenced with the JTTR and the ASBPO Blood Bank transfusion record. Discrepancies were resolved by reconciling the times and locations recorded on blood transfusion slips, anesthesia records, intensive care unit (ICU) records, operative reports, and discharge summaries. Discrepancies typically arose from missing or incomplete blood transfusion slips, double counting of carbon copies of blood transfusion slips, incorrect documentation of blood products (e.g., FFP recorded as aPLT), inaccurate documentation in anesthesia reports, or inaccurate attribution of emergency release blood products to a particular recipient by the blood bank. Dual examiner comparison of multiple data sources and correlation to patient medical records ensured data accuracy and fidelity.

Data Collection

Once patients were screened for inclusion and exclusion criteria, the following characteristics were captured: age, sex, admission vital signs, Glasgow Coma Scale (GCS) score, admission laboratory tests, mechanism of injury, documented injuries, 6-hour and 24-hour blood product administration (RBC, FFP, cryo, and aPLT), and recombinant factor VIIa (rFVIIa) administration and dose. Plasma ratios were calculated as (FFP/RBC), and aPLT ratios were calculated as (aPLT/RBC). Admission vital signs were used to calculate Revised Trauma Scores (RTSs).[17] Abbreviated Injury Scale scores and Injury Severity Scores (ISSs) were centrally scored and calculated by the research nurses and staff of the JTTR using ISS-98 after patient discharge.[18]

The primary outcomes evaluated were survival at 24 hours and at 30 days. Survival of United States soldiers was ascertained by tracking their progress through evacuation and higher *echelons* of care. Foreign National casualties who were discharged before 30 days were lost to follow-up unless they were seen as outpatients in follow-up or were readmitted to the combat hospital. Secondary outcomes, including causes of death from central nervous system injury, exsanguination, airway failure, multisystem organ failure (in patients surviving longer than 24 hours), venous thromboembolism, and air embolism were also evaluated.

Statistical Analysis

Baseline characteristics, blood product transfusion timing and location, rFVIIa usage, and survival at 24 hours and at 30 days were compared between groups. Data were evaluated for normality using Kolmogorov-Smirnov, Shapiro-Wilk, and

normality plots. Analysis of variance was used to compare parametric data between groups, whereas Kruskal-Wallis and pairwise Mann-Whitney *U* test were used to compare nonparametric data between groups. The Pearson χ^2 test was used to compare dichotomous variables between groups. To adjust for potential confounders, we constructed Cox proportional hazards models of 24-hour and 30-day survival for baseline variables, excluding variables subsumed within other variables (e.g., systolic blood pressure [SBP], respiratory rate, and GCS are used to calculate RTS). Baseline and resuscitation variables were assessed for effect on survival by univariate analysis (Kruskal-Wallis test). Factors influencing survival on univariate analysis were included in Cox proportional hazards models of 24-hour and 30-day survival. Kaplan-Meier survival curves were plotted for LOW versus HIGH groups. Continuous data are presented as median (interquartile range) mean. Differences were considered statistically significant when $p \leq 0.05$ for all group comparisons. Statistical analysis was performed with SPSS 17.0 (Chicago, IL).

RESULTS

During the 36-month period between January 2004 and December 2006, the CSH received 8,618 injured patients, of which 2,024 (23%) were transfused, with 694 (8.1%) identified as having received an MT. Two hundred eighty patients were excluded from the analysis: 18 patients underwent an MT during their hospital course and not within 24 hours of admission, 84 patients were transferred from outside facilities, 134 patients received FWB, 30 presented with incomplete medical records, and 14 died within 1 hour of admission. Of 414 patients remaining, 344 were transfused 1:10 or less aPLT units per 10 units of RBC units (LOW group); 70 were transfused more than 1:10 aPLT units per 10 units of RBC (HIGH group).

TABLE 1. Demographic and Admission Variables of LOW and HIGH 6-Hour Platelet Groups

Variable	LOW (≤1:10) 6-h aPLT/RBC (n = 344)	HIGH (>1:10) 6-h aPLT/RBC (n = 70)
	Median (IQR) mean	Median (IQR) mean
Age, y	26 (21 31) 28	26 (21 31) 28
Sex (male), %	99	93*
ISS	20 (12 28) 23	25 (18 32) 24
RTS	6.5 (5.6 7.4) 7.1	6.6 (5.7 7.5) 7.1
Penetrating injury, %	93	89
Admission vital signs		
Pulse, beats/min	120 (103 137) 115	125 (112 138) 124*
Respirations, breaths/min	22 (18 26) 23	22 (16 28) 24
T, °C	36.4 (35.7 37.1) 36.2	36.7 (36.2 37.3) 36.6*
SBP, mm Hg	99 (77 121) 103	100 (80 120) 100
GCS	15 (14 15) 13	15 (13 15) 12
Admission laboratory results		
Base deficit, mmol/L	7 (4 11) 8	8 (3 13) 10*
Hemoglobin, g/dL	11.5 (9.5 13.5) 11.3	11.7 (10.6 12.8) 11.4
Platelet count, 1,000 s/mm^3	270 (194 346) 275	242 (169 315) 254
INR	1.4 (1.1 1.7) 1.6	1.6 (1.3 2.0) 1.9*

Mann-Whitney *U* test or χ^2: * $p < 0.05$.
IQR, interquartile range.

TABLE 2. 6-Hour Use of Blood Components and Factor rVIIa in the LOW and HIGH aPLT/RBC Patients

Component (Units)	LOW	HIGH
	Median (IQR) mean	Median (IQR) mean
RBC	13 (8 18) 16	16 (11 22) 18*
Plasma	8 (4 12) 9	12 (10 15) 12*
Platelets	0.00 (0 1) 0.64	2.00 (1 3) 2.43*
Cryoprecipitate	0 (0 10) 5	10 (9 11) 12*
Plasma:RBC	0.55 (0.38 0.73) 0.56	0.70 (0.56 0.84) 0.71*
Platelet:RBC	0.00 (0.00 0.07) 0.03	0.13 (0.12 0.15) 0.14*
Factor rVIIa yes/no, %	55	79*
Factor rVIIa dose, mg	4.8 (0.0 7.2) 5.2	7.2 (0.0 12.0) 9.5*

Mann-Whitney *U* test or χ^2: *all comparisons significant with $p < 0.01$.
IQR, interquartile range.

Characteristics of the Patients

The groups were similar (Table 1) based on admission demographics, ISS, RTS, vital signs, and laboratory studies. The patients were young (median age, 26 years), male (>90%), with median ISS 20 to 25, and most presented with penetrating injuries (≈90%). There were differences between groups for admission vitals (HIGH, more tachycardic, pulse 125 beats/min vs. 120 beats/min; HIGH with higher temperature [*T*], 36.7 vs. 36.4°C) and laboratory results (HIGH with more severe shock, base deficit 8 vs. 7; HIGH more coagulopathic, International Normalized Ratio [INR]) 1.6 vs. 1.4). There were differences between groups in resuscitation management (Table 2); but in general, the LOW group received fewer RBC, FFP, aPLT, and cryoprecipitate units as well as a lower FFP:RBC ratio compared with the HIGH group ($p < 0.01$ for all pairwise comparisons). The proportion of patients receiving rFVIIa differed between groups (79% HIGH, 55% LOW), and the dose of rFVIIa was higher in the HIGH group (median, 7.2 mg) compared with

TABLE 3. Patients Receiving ED Blood Components in the LOW and HIGH aPLT/RBC Groups

Component (Units)	LOW	HIGH
	n (%)	n (%)
RBC	287/344 (83)	64/70 (91)
Plasma	97/344 (28)	37/70 (54)*
Platelets	8/344 (2)	12/70 (17)*
Cryoprecipitate	0/344 (0)	2/70 (3)*
	Median (IQR) mean	Median (IQR) mean
Mean time to operating room, h	0.8 (0.6 1.4) 1.0	0.7 (0.4 1.1) 1.1

Mann-Whitney *U* test *or* χ^2: *all comparisons were significant with $p < 0.01$.
IQR, interquartile range.

TABLE 4. Mortality Rates and Causes in the LOW and HIGH aPLT/RBC Patients

Outcome	LOW	HIGH
	n (%)	n (%)
24-h survival	268/344 (78)	*63/70 (90)
30-d survival	245/344 (71)	†57/70 (81)
Cause of death		
CNS injury	16/97 (16.5)	2/13 (15.4)
Truncal hemorrhage	59/97 (60.8)	‡3/13 (23.1)
Airway	3/97 (3.1)	‡2/13 (15.4)
MOFS	16/97 (16.5)	‡6/13 (46.2)
Venous thromboembolism	1/97 (1.0)	0/13 (0.0)
Air embolism	2/97 (2.1)	0/13 (0.0)

χ^2: *p 0.02, †p 0.08, ‡$p < 0.05$.
Total deaths 112: LOW 99 (2 with cause of death undetermined), HIGH 13.

the LOW group (median, 4.8 mg, $p < 0.01$ for pairwise comparisons). Not only did the HIGH group receive resuscitations with greater hemostatic capacity, but the products were administered earlier (Table 3). Fifty-four percent of the HIGH group received FFP in the emergency department (ED) compared with 28% in the LOW group. Seventeen percent of patients in the HIGH group received platelets in the ED compared with 2% in the LOW group. Three percent of the HIGH group received cryoprecipitate in the ED compared with no patients in the LOW group (all with $p < 0.01$). By contrast, there were no significant differences between HIGH and LOW groups with regard to time-to-operating room (OR) (0.7 hours and 0.8 hours, respectively).

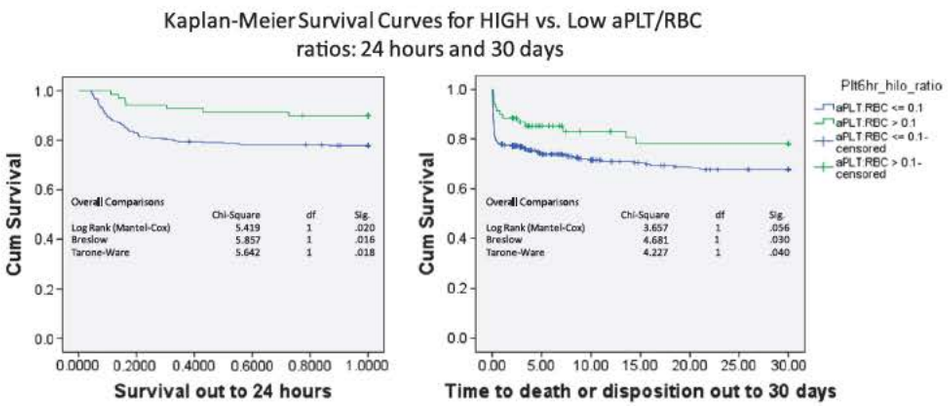
Outcomes

The primary outcome of survival (Table 4) at 24 hours was 78% in the LOW group and 90% in the HIGH group (χ^2 $p = 0.02$), and most deaths in the first 24 hours occurred within 6 hours of admission (Fig. 1). Differences between groups diminished with 30-day survival (LOW group 71% vs. HIGH group 81%, $p = 0.08$, χ^2; significance borderline by Kaplan-Meier analysis). Overall mortality was 27% (n = 112: LOW = 99, HIGH = 13). One hundred fifty-four patients were lost to follow-up (non–United States nationals); 260 patients remained in the analysis at 30 days. Of the 71 patients who died in the first 6 hours (63% total mortality), only 4 (6%) received aPLT in the ED, 28 (39%) received aPLT in the OR, and 33 (46%) received any platelets before dying; only 4 (6%) were in the HIGH group. In the LOW group, 67 (68%) of 99 total deaths occurred in the first 6 hours compared with 4 (31%) of 13 total deaths in the HIGH group.

Regarding secondary outcomes, exsanguination caused by truncal hemorrhage represented 60.8% of evaluable deaths in the LOW group compared with 23.1% in the HIGH group ($p < 0.05$). Airway deaths were more common in the HIGH group (15.4 vs. 3.1% LOW, $p < 0.05$). Similarly, multi-organ failure syndrome (MOFS) was more common in the HIGH group (46.2 vs. 16.5% LOW, $p < 0.05$). Rates of death caused by venous thromboembolism, air embolism, and central nervous system injury were similar between groups.

Demographic characteristics, admission vital signs, and laboratory values, as well as resuscitation variables, were assessed for effect on survival by univariate analysis (Kruskal-Wallis test). The following variables were tested: age, sex, percentage of penetrating injury, ISS, RTS, heart rate, *T*, platelet count, hemoglobin, base deficit, INR. The following were found to be associated ($p < 0.05$) with survival and were included in multivariate analyses of survival: percentage of penetrating, ISS, RTS, *T*, platelet count, hemoglobin, and base deficit. We also tested the following resuscitation variables: aPLT ratio group (LOW, HIGH), plasma ratio, 24-hour cryoprecipitate dose, Factor VII use (yes vs. no), and dose. The aPLT ratio group and plasma ratio variables were significantly associated with survival in the univariate analysis ($p < 0.05$) and were included in multivariate analyses.

Variables independently associated with increased mortality (Table 5) at 24 hours included ISS (hazard ratio [HR] 1.065) and being in the LOW instead of the HIGH group (HR, 4.254; i.e., being in the LOW group was associated with a 4.254-fold higher hazard of death during 24 hours than being in the HIGH group). Variables independently associated with decreased mortality at 24 hours included RTS (HR,



24 hr and 30 day survival curves by Platelet Ratio Group

Figure 1. The 24-hour and 30-day survival curves by the Platelet Ratio Group.

TABLE 5. Hazard Ratios Predicting 24-Hour and 30-Day Survival: Cox Proportional Hazards Models

Variable	24-H Survival Hazard Ratio (95% confidence interval)	*p*	30-D Survival Hazard Ratio (95% confidence interval)	*p*
Penetrating injury, %	0.681 (0.230 2.016)	0.488	0.841 (0.340 2.079)	0.707
ISS	1.065 (1.037 1.093)	0.001*	1.052 (1.031 1.074)	0.001*
RTS	0.837 (0.712 0.984)	0.031*	0.805 (0.709 0.914)	0.001*
T, °C	0.975 (0.780 1.218)	0.822	1.041 (0.863 1.255)	0.676
INR	1.142 (0.949 1.375)	0.159	1.198 (0.987 1.382)	0.071
Platelet count,1,000 s/mm^3	0.999 (0.996 1.002)	0.530	1.000 (0.998 1.002)	0.858
Hemoglobin, g/dL	0.939 (0.828 1.065)	0.328	1.012 (0.920 1.114)	0.807
Base deficit, mmol/L	1.045 (0.992 1.100)	0.094	1.038 (0.996 1.081)	0.077
Plasma:RBC	0.035 (0.009 0.127)	0.001*	0.217 (0.082 0.575)	0.002*
Platelets LOW vs. HIGH	4.254 (1.249 14.484)	0.021*	2.319 (1.110 4.843)	0.025*

*Significant ($p < 0.05$) predictors of mortality on multivariate analysis at 24 hours and 30 days.

0.837) and plasma ratio (HR, 0.035). Variables independently associated with increased mortality at 30 days included ISS (HR, 1.052) and being in the LOW instead of the HIGH group (HR, 2.319). Variables independently associated with decreased mortality at 30 days included RTS (HR, 0.805) and plasma ratio (HR, 0.217).

DISCUSSION

This article represents the largest analysis examining the impact of platelet ratios transfused within the first 6 hours in massively transfused combat casualties with penetrating injury published to date. Our results corroborate what has been noted in civilian literature: that the early use of both platelets and plasma may be vital in managing massively transfused trauma patients.[14] Clinically relevant thrombocytopenia has previously been considered a delayed complication of MT based on data from the era of stored whole-blood transfusion, which showed that circulating platelet counts dropped to less than $50 \times 10^3/\text{mm}^3$ only after multiple blood volume replacements.[19] However, assumptions of "clinically relevant thrombocytopenia" do not take into account platelet dysfunction in trauma caused by acidosis, hypothermia, outpatient medications with activity against platelets (such as aspirin/nonsteroidal anti-inflammatory drugs or clopridogrel) or other as yet undetermined factors.[20]

The optimal timing of platelet administration has not been clearly defined. Given that most deaths in our study occurred by 6 hours, it would be appropriate to examine this more closely with time-covariate adjusted analyses. This was not possible because of limitations in the underlying data. Our analysis does show that patients receiving a more hemostatic resuscitation (HIGH group) received more hemostatic products in the ED and thus earlier than patients in the LOW group. This may have contributed to improved survival and also possibly to the reduced rate of death because of truncal hemorrhage in the HIGH group. It should be noted that the increase in MOFS seen in the HIGH group corroborates this suggestion because MOFS, a late complication, is fundamentally a disease of survivorship. Based on these findings, it is tempting to speculate that prehospital hemostatic resuscitation, incorporating platelets, or platelet-derived products may further improve survival in trauma.

The optimal ratio of platelets to administer during an MT has also not been precisely defined. We chose more than 1:10 aPLT:RBC as the HIGH platelet ratio group based on previously published data.[4,14,21,22] Prospective studies are needed to analyze the optimal empiric ratio or, perhaps more appropriately, if rapid laboratory methods capable of estimating platelet function can be used to analyze the need for platelets.

This is a retrospective analysis, in which clinical decisions were made at the bedside and treatment groups were not assigned. The data presented here are hypothesis generating; they only show an association between whether patients received a high or low ratio of platelets and survival. These data cannot be used to make definitive conclusions about the best management for trauma casualties. Our analysis was limited by inability to perform time-covariate analysis that could further adjust for survival bias. Our exclusion of patients who died within 1 hour reduces the risk of survivorship bias but does not eliminate it. The fact that 154 of 414 patients were lost to follow-up at 30 days may also introduce bias. These patients were non-United States nationals for whom post-discharge information was unavailable. The exclusion of patients receiving less than 10 units of blood in 24 hours may have introduced bias because these patients may have died before being able to receive 10 units, although it is also unlikely that such patients received platelets. An additional limitation is the inability to adjust for crystalloid and colloid volume administration.[23] This was caused by the inaccuracy of the volumes recorded in our databases discovered during data validation audits. The large volume and rapidity at which these fluids are given in a combat setting, where personnel resources required to document are limited, likely contributed to the inaccuracy of these data. Our analysis is also limited because we did not report outcomes such as ventilator

days, ICU days, or hospital length of stay. Finally, the findings of this study are limited to patients receiving an MT in the setting of trauma and may not be applicable to patients undergoing elective surgery or patients expected to receive less than 10 units of blood.

In conclusion, increased platelet:RBC and plasma:RBC ratios are associated with increased survival in the setting of MT. Early transfusion of hemostatic products, in the ED, may also contribute to improved survival. Our findings support the development of prospective clinical trials that will analyze the optimal timing of platelet administration in patients with life-threatening hemorrhage from trauma. Until such data are available, early transfusion of platelets should be considered an integral component in the management of trauma patients requiring massive transfusion.

AUTHORSHIP

A.P.C. was the primary author, in charge of data gathering, analysis and writing. J.G.P. contributed to data gathering, analysis and writing. M.A.B. contributed to data analysis. P.C.S. and L.H.B. contributed to data analysis and writing.

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DISCLOSURE

The authors declare no conflicts of interest.

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